

REMARKS

STATUS OF THE CLAIMS

Claims 1-140 are currently pending in the application. Of such claims, 1-18, 41, and 64-140 are withdrawn from current consideration. Of the currently considered claims, claims 22 and 45 were rejected under 35 U.S.C. §112, first paragraph as allegedly lacking enablement; claims 19-40 and 42-63 were rejected under 35 U.S.C. §112, second paragraph as allegedly indistinct; claims 19, 22-23, 26-29, 32-33, 35-39, 42, 45-46, 49-52, 55-56, and 58-59 were rejected under 35 U.S.C. §102(a) or (b) as purportedly anticipated by Morigaki *et al.* (2001, *Angew. Chem. Int. Ed.*, 40(1):172-174); claims 30-31, 34, 40, 53-54, 57, and 60-63 were rejected under 35 U.S.C. §103(a) as allegedly obvious in light of Morigaki, *supra*; claims 20-21, 43-44, and 61-63 were rejected under 35 U.S.C. §103(a) as allegedly obvious in view of Morigaki in light of Cremer (1999, *J. Am. Chem. Soc.*, 121:8130-8131); and claims 24-25, and 47-48 were rejected under 35 U.S.C. §103(a) as allegedly obvious in view of Morigaki in view of Ulman (1997, *Advanced Matter*, 9(14):1121-1123). Claims 19, 21, 42, and 44 are amended herein to more clearly describe embodiments of the invention, while claims 30 and 53 are cancelled. These changes introduce no new matter and support is present in the application as originally filed. The changes are made without prejudice and are not to be construed as abandonment of any previously claimed subject matter or agreement with any objection or rejection of record. Accordingly, entry of the Amendment is respectfully requested.

REJECTIONS TO THE CLAIMS

35 U.S.C. §112 First Paragraph.

Enablement

Claims 22 and 45 were rejected in the current Office Action under 35 U.S.C. §112, first paragraph as allegedly lacking enablement for the terms “tethered lipid bilayer,” “polymer-cushioned lipid bilayer,” “...in a proteo-lipidic mixture,” and “hybrid lipid bilayer . . . and an inner self-assembly monolayer.” Applicants respectfully traverse.

M.P.E.P. §2164.01 instructs that,

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures

in the patent *coupled with information known in the art*
without undue experimentation. (Emphasis added.)

The same M.P.E.P. section also states that a “patent need not teach, and preferably omits what is well known in the art.”

Applicants submit that the above terms are well recognized by those of skill in the art. Those of skill would be aware of, and familiar with, various different tethered lipid bilayers, polymer cushioned lipid bilayers, proteo-lipidic mixtures, and hybrid bilayers, and would easily understand, and not miscomprehend, the description in the specification. Such terms are not unknown biological constructs that ordinarily skilled artisans would easily miscomprehend.

The specification as filed describes on page 26, that “[t]ethered lipid membranes (or tethered lipid bilayers, tethered bilayers, etc.) typically comprise bilayer membranes separated from a supporting substrate by low molecular weight spacers such as peptides or polyoxyethylene (PEG) groups.” Additional descriptions of exemplary tethered lipid bilayers or membranes can be found in, *e.g.*, Sinner, *et al.*, 2001, “Functional tethered membranes,” *Current Opinions in Chemical Biology* 5(6):705-711, (listed in IDS of September 30, 2004) and the multiple references cited therein. Additionally, a PubMed search of scientific journals (www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed) for “tethered lipid bilayers,” and similar phrases, returns numerous citations published prior to the filing date (and the priority date) of the current application.

The specification as filed also describes on page 26, that “[p]olymer-cushioned lipid bilayers (or polymer-supported lipid bilayers) are typically separated from a supporting substrate by, *e.g.*, carbohydrate functionalized lipopolymers, or the like, and typically have a greater distance between the bilayer and the underlying substrate than do tethered bilayers.” Additional descriptions of exemplary polymer cushioned lipid bilayers, can be found in, *e.g.*, Sackmann, *et al.*, 2000, “Supported membranes on soft polymer cushions: fabrication, characterization and applications,” *Trends in Biotechnology*, 18:58-64, (listed in IDS of September 30, 2004) and the multiple references cited therein. Additionally, a PubMed search of scientific journals for “cushioned lipid bilayers” and similar phrases (*see above* for URL) returns multiple citations published prior to the filing date (and priority date) of the current application.

The specification as filed, also on page 26, describes that “[p]roteo-lipidic mixtures are mixes of proteins and various lipid moieties” without limitation as to specific proteins or specific

lipid moieties. Thus, proteo-lipidic mixtures comprise, *e.g.*, proteins within and associated with lipid bilayers. Figure 12 in the application as filed displays a schematic representation of various exemplary proteins within an exemplary lipid bilayer. The concept of myriad and diverse proteins (and other molecules) within and associated with lipid bilayers (of various compositions) is a bedrock concept of cellular biology and is extremely well known by those of skill in the art. An additional exemplary, but not limiting, schematic of a lipid bilayer, a cell membrane, (1989, Curtis, *et al*, Biology, 5th Edition, Worth Publishers, Inc., New York) is attached showing proteins within and associated with a lipid membrane (again, a cell membrane in this example).

The term “hybrid lipid bilayer . . . and an inner self-assembly monolayer” is described on page 26, paragraph 64 as comprising, “*e.g.*, one lipid layer that is from one source or is naturally occurring and another layer that is from another source or is, *e.g.*, a self-assembled monolayer.” Additionally, Figure 3 in the as-filed application shows a schematic diagram showing an exemplary hybrid bilayer comprising an inner leaflet of covalently tethered alkylsilane monolayer and an outer leaflet of a phospholipid. Such hybrid bilayers are well known to those of skill in the art. For example, Plant described such structures in 1999 in “Supported Hybrid Bilayer Membranes as Rugged Cell Membrane Mimics,” *Langmuir*, 15:5128-5135. Similar constructs are described within the numerous citations therein and in, *e.g.*, Tarek, *et al.*, “Molecular Dynamics Simulations of Supported Phospholipid/Alkanetiol Bilayers on a Gold(111) Surface,” *Biophysical Journal*, 77:964-972.

Thus, Applicants submit that the above terms (“tethered lipid bilayer,” “polymer-cushioned lipid bilayer,” “...in a proteo-lipidic mixture,” and “hybrid lipid bilayer . . . and an inner self-assembly monolayer”) are, not only adequately described in the specification, but are terms well known to those of skill in the art and are therefore sufficiently described in the specification in terms that would allow one reasonably skilled in the art to make or use the invention. Because of the above reasons, Applicants respectfully request that the rejection be withdrawn.

35 U.S.C. §112 Second Paragraph.

Claims 19-40 and 42-63 were rejected under 35 U.S.C. §112, second paragraph as allegedly being indefinite by failing to particularly point out and distinctly claim the subject matter regarded by applicants as the invention. Applicants amend in part and traverse in part.

M.P.E.P. §2173.02 instructs that determination of indefiniteness is analyzed through examination of the content of the disclosure, the teachings of the prior art, and the interpretation that one possessing the ordinary level of skill in the art would give. In sum, the language must be such that a person of ordinary skill in the art could interpret the metes and bounds of the claim. Paraphrasing *Morton Int'l, Inc. v. Cardinal Chem. Co.*, 5F.3d 1464, 1470, 28 USPQ2d 1190, 1195 (Fed. Cir. 1993).

The Office Action rejected the same terms as allegedly indefinite as it rejected as allegedly lacking enablement (*i.e.*, “tethered lipid bilayer,” “polymer-cushioned lipid bilayer,” “...in a proteo-lipidic mixture,” and “hybrid lipid bilayer . . . and an inner self-assembly monolayer”). Applicants respectfully traverse.

As explained above, the terms “tethered lipid bilayer,” “polymer-cushioned lipid bilayer,” “...in a proteo-lipidic mixture,” and “hybrid lipid bilayer . . . and an inner self-assembly monolayer” are ones that are well known by those of skill in the art (at the time of filing). The level of skill in the field is high and the teachings of the prior art are quite available, both as evidenced by the numerous references cited, etc. The terminology used in the application and the descriptions given, would therefore easily allow those of ordinary skill in the art to interpret the metes and bounds of the current claims. Therefore, since the terms are such that those of skill in the art could interpret the metes and bounds of the claims, they are not indefinite and Applicants respectfully request that the rejection be withdrawn.

The Office Action also rejected claims 20-21 and 43-44 as allegedly unclear as to whether the plurality of masks and secondary bilayers/materials are used simultaneously or sequentially and whether such pluralities were applied to the same primary lipid bilayer or to different primary lipid bilayers. Applicants herein amend.

Claims 21 and 44 are amended to read “sequentially repeating steps [[i]] ii-vi for substantially all members of the plurality.” Such changes are to emphasize that in the current embodiments, the same primary lipid bilayer(s) is to be subjected to multiple rounds of masking, etc. Of course, it is not to be construed that Applicants are disclaiming embodiments comprising simultaneous use of masks or multiple primary bilayers. Support for the changes is replete throughout the application and figures as filed. For example, paragraph 87 on page 40 discusses multiple rounds of patterning and refunctionalization of a single primary bilayer. Because the

allegedly indefinite language in the claims upon which the rejection is based has been modified, Applicants respectfully request that the rejection be withdrawn.

Claims 30 and 53 were also rejected in the current Office Action for alleged indefiniteness of “adjustable.” Applicants herein cancel claims 30 and 53.

While Applicants believe that the term “adjustable” is not indefinite as used in the current application, in order to further prosecution, claims 30 and 53 are cancelled herein. Because the allegedly indefinite claims are cancelled, Applicants respectfully request that the rejections be withdrawn.

Finally, claims 19 and 42 were rejected for alleged indefiniteness for subclaim (iv). The Office Action purports that the claim does not state how the UV-transparent mask areas correspond to the lipid-free areas created in the bilayers. Applicants herein amend.

As detailed directly below in the next section, Applicants herein amend claims 29 and 42 to more clearly define the current embodiment. Thus, the amended language makes more clear that the lipid-free areas or “holes” in the primary bilayer are underneath the UV-transparent areas of the mask. The holes thus spatially correspond with the UV-transparent areas. Because the allegedly indefinite language in the claims upon which the rejection is based has been modified, Applicants respectfully request that the rejection be withdrawn.

35 U.S.C. §102(b).

Morigaki

Claims 19, 22-23, 26-29, 32-33, 35-39, 42, 45-56, 49-52, 55-56, and 58-59 were rejected under 35 U.S.C. §102(b) (or alternatively under 35 U.S.C. §102(a)) as allegedly anticipated by Morigaki *et al.* (2001, *Agnew. Chem. Int. Ed.*, 40(1):172-174). Applicants herein amend.

While Applicants believe that Morigaki does not disclose all of the elements of the unamended claims, in order to further prosecution and to more clearly lay out the parameters of the currently claimed embodiments, Applicants herein amend claims 19 and 42 (and hence their dependents 20-41 and 43-63), to recite:

iv) creating in the primary lipid bilayer, one or more non-lipid areas beneath the one or more UV transparent areas of the UV-opaque mask, by exposing the primary lipid bilayer to UV light through the one or more patterned UV-opaque mask, thereby constructing one or more patterned lipid bilayer, which patterned lipid bilayer

comprises the one or more non-lipid areas which spatially correspond to the one or more UV-transparent areas in the UV mask.

Support for such change is replete throughout the application as filed. *See, e.g.*, paragraphs 57-58 and Figure 1. The changes to claims 19 and 42 do not present new matter and their entry is respectfully requested.

In order for a reference to anticipate a claim “the reference must teach every element of the claim.” M.P.E.P. §2131. Applicants respectfully submit that Morigaki does not teach every element of amended claims 19 and 42 (and hence does not present every element of claims 22-23, 26-29, 32-33, 35-39, 45-56, 49-52, 55-56, and 58-59 which depend from claims 19 and 42). For example, Morigaki does not teach methods wherein areas are cleared in a lipid bilayer by removal with UV light.

In fact, Morigaki is actually quite different from the current invention. In Morigaki the bilayers are arguably “patterned” by exposing a polymerizable lipid bilayer to UV through a mask. However, and quite importantly, the UV in Morigaki is not used to create non-lipid (or empty) areas within the bilayer. Rather, the UV in Morigaki is used to create polymerized areas. Again, the UV in Morigaki does not create the lipid free “hole” areas. *See*, Morigaki Figure 1 and page 172.

Therefore, the method in Morigaki is completely opposite of that of the current invention which uses UV to create empty areas or holes within a lipid bilayer. While Applicants believe that the unamended claims cover such action, claims 19 and 42 (subclaim iv) are amended herein to make such action more explicit.

Because Morigaki does not present all of the elements of amended (or unamended) claims 19 and 42 (and hence their dependents as well), it cannot anticipate the current invention and Applicants respectfully request that the rejection be withdrawn.

35 U.S.C. §103(a).

A *prima facie* case of obviousness from combined references requires that the combination of the cited art, taken with general knowledge in the field, must supply all of the elements of the claimed invention. M.P.E.P. §2143.03. Additionally, there must be a motivation or suggestion to modify the reference(s) or combine the teaching(s) to produce the claimed invention. M.P.E.P. §2143.01 and *In re Geiger*, 815 2 USPQ2d 1276, 1278 (Fed. Cir. 1987). Furthermore,

there must be a reasonable expectation of success. M.P.E.P. §2143.02 and *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991), citing *In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed Cir. 1988). The required teaching or suggestion to combine the references, and the expectation of success, must both be found in the prior art and not based upon the disclosure of the Applicants. M.P.E.P. §2142. Applicants respectfully point out that these requirements have not been met for a *prima facie* showing of obviousness for combinations of the cited references.

Morigaki

Claims 30-31, 34, 40, 53-54, 57, and 60-63 were rejected under 35 U.S.C. §103(a) as allegedly obvious in view of Morigaki. Applicants respectfully traverse.

As detailed above, Morigaki does not contain all of the elements of the current claims. The Office Action suggests five additions from common knowledge to the teachings of Morigaki. Namely, the Office Action suggests: addition of adjustable UV light source, addition of 254 nm UV light source, addition of particular patterns and density/size/number of patterns, addition of contiguous patterning, and addition of arrays for combinatorial chemistry.

As stated above, Morigaki does not contain all elements of the current claims since, *e.g.*, it does not involve teachings such as those present in current subclaim iv in claims 19 and 42 (and hence their dependents as well) which require creation of non-lipid areas within a lipid bilayer resulting from UV exposure through UV-transparent areas in a UV-opaque mask. The addition of the five above suggested additions (*e.g.*, adjustable, etc.) does not remedy this lack. Even with the suggested additions, Morigaki does not involve use of UV light through a mask to produce lipid free areas and, thus, does not present all elements of the current claims. Therefore Morigaki cannot render the invention obvious. Applicants, therefore, respectfully request that the rejection be withdrawn.

Morigaki and Cremer

Claims 20-21, 43-44, and 61-63 were rejected in the current Office Action under 35 U.S.C. § 103(a) as allegedly obvious in view of Morigaki in light of Cremer (1999, *Journal of the American Chemistry Society*, 121:8130-8131). Applicants respectfully traverse.

Again, as detailed above, Morigaki does not contain all of the elements of current claims 19 and 42 (and hence their dependents as well), *e.g.*, Morigaki does not involve creation of non-lipid areas within a lipid bilayer from UV exposure through UV-transparent areas in a UV-

opaque mask. Furthermore, even with the additional teachings alleged by the Office Action from Cremer, the combination of Morigaki and Cremer still does not teach all of the elements of current amended claims 19 and 42 and their dependents.

The Office Action cites Cremer for its supposed teachings of: combinatorial chemistry, application of plural lipid bilayers, use of multiple UV masks, and repetition of steps. However, none of these teachings, and indeed none of the teachings in Cremer as a whole, supply the necessary elements of creation of non-lipid areas within a lipid bilayer from UV exposure through UV-transparent areas in a UV-opaque mask as is required by current claims 19 and 42 and their dependents.

Thus, because the combination of Morigaki and Cremer does not present all elements of the current claims and, thus, cannot render the invention obvious, Applicants respectfully request that the rejection be withdrawn.

Morigaki and Ulman

Claims 24-25 and 47-48 were rejected in the current Office Action under 35 U.S.C. §103(a) as allegedly obvious in view of Morigaki in light of Ulman (1997, *Advanced Matter*, 9(14):1121-1123). Applicants respectfully traverse.

Once more, as detailed above, Morigaki does not contain all of the elements of current claims 19 and 42 (and hence their dependents as well), *e.g.*, Morigaki does not involve creation of non-lipid areas within a lipid bilayer resulting from UV exposure through UV-transparent areas in a UV-opaque mask. Furthermore, even with the additional teachings alleged by the Office Action from Ulman, the combination of Morigaki and Ulman still does not teach all of the elements of current amended claims 19 and 42 or their dependents.

The Office Action cites Ulman for its supposed teachings of use of 3D or non-planar membranes. However, such teachings, and indeed none of the teachings in Ulman as a whole, supply the necessary elements of creation of non-lipid areas within a lipid bilayer resulting from UV exposure through UV-transparent areas in a UV-opaque mask as is required by current claims 19 and 42 and their dependents.

Thus, because the combination of Morigaki and Ulman does not present all elements of the current claims and, thus, cannot render the invention obvious, Applicants respectfully request that the rejection be withdrawn.

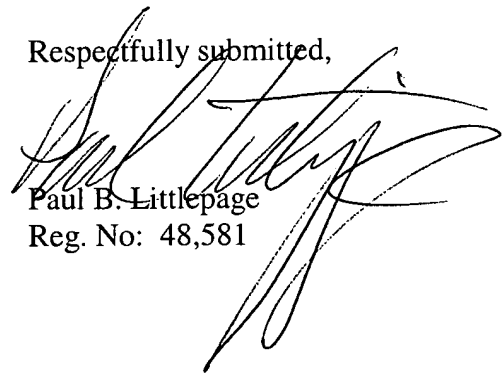
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CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. In the event that substantive matters are felt to remain, the Examiner is invited to telephone the undersigned at (510) 769-3507.

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